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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	**Confirmation No. 3474**
Takashi GOTO et al.	:	Docket No. 2000_0578A
Serial No. 09/530,702	:	Group Art Unit 1655
Filed May 4, 2000	:	Examiner J. Taylor

HEPARIN COFACTOR II PREPARATION AND PROCESS THEREFOR

AMENDMENT

Assistant Commissioner for Patents,
Washington, D.C.

Sir:

Responsive to the Official Action dated December 19, 2001, the time for responding thereto being extended for one month in accordance with a petition for extension submitted concurrently herewith, please amend the above-identified application as follows:

IN THE CLAIMS

Kindly amend the claim as follows:

18. **(Amended)** A method for producing a heparin cofactor II-containing preparation substantially free of a degrading factor according to claim 12, comprising a step of separating heparin cofactor II and a degrading factor from a solution containing the heparin cofactor II and the degrading factor, to obtain the heparin cofactor II-containing preparation substantially free of the degrading factor.

A1

Please add the following new claim:

36. **(New)** The heparin cofactor II-containing preparation of claim 15, wherein a genome of the infective virus is not detected by the PCR method.

A2

REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

The Examiner indicates that the restriction requirement is maintained, because the claims of Group II are drawn to a production method which method is not required to obtain the product of Group I. However, the method claims are intended to obtain the product of claim 12. Claim 18 has accordingly been amended to clarify this relationship. In view of the foregoing, it is respectfully submitted that method claims 18-35 should be rejoined with the elected product claims 12-17 upon an indication of allowability of the product claims, under customary PTO practice.

New claim 36 has been added for additional patent protection. This claim is supported by Experimental Example 1 in the specification.

The Official Action contains a single ground of rejection. Claims 12-17 are rejected under 35 USC 102 as being anticipated by Griffith et al. This ground of rejection of respectfully traversed.

The cited reference states, "Since the degraded-heparin cofactor II was obtained only when the PEG fractionation step was replaced by a heparin-agarose batch adsorption step, it appeared that the protease was present in the barium citrate adsorbed plasma, but was separated from heparin cofactor II by PEG fractionation." See page 2224, lines 7-3 from the bottom of the page. This means that the cited reference presumes that protease was separated from HCII by PEG fractionation because degraded HCII was not obtained by this process. However, the truth was that the degraded HCII was not obtained because it had been removed by PEG fractionation, rather than protease.

This is evident from the fact that high concentration (10mM) of DFP (potent serine protease inhibitor) was added to HCII pool in the cited reference. See page 2224, lines 3-1 from the bottom of the page. This means that the authors of the cited reference considered that the HCII pool might be contaminated with protease, notwithstanding the earlier.

Furthermore, the cited reference also teaches that the treatment of the HCII pool with 10 mM DFP could not inhibit subsequent degradation. See page 2224, lines 3-1 from the bottom of the page. This means that some degrading factor that could not be inhibited by DFP still remained in the HCII pool. Please refer to the enclosed printout from the website "PROLYSIS" and the corresponding page of SIGMA catalog for detailed information about DFP. From the foregoing, it is evident that the HCII preparation of the cited reference contains degrading factor, unlike the HCII preparation of the present invention, and the present invention is not anticipated by this reference.

The Examiner also states that the purified HCII of the cited reference was free of an infective virus. This is not correct, because only A280 and HCII activity were determined in the cited reference (e.g., Figure 3). Viruses are not detected through HCII activity, and may not be detected by absorbance at 280 nm. In the present invention, therefore, viral genomes are detected, preferably by the PCR method, based on which the substantial absence of viruses is confirmed.

Attached hereto is a marked-up version of the changes made to the claim by the current amendment. The attached page is captioned "**Version with markings to show changes made**."

In view of the foregoing, favorable reconsideration and allowance is respectfully solicited.

Respectfully submitted,

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